I. REMARKS

Interview request

Applicants thank the Examiner for agreeing to an interview for the instant application, which at the time of filing of this response is scheduled for Thursday, August 26th, 2004, at 11:00 am (eastern time) at the USPTO, with Examiner Richard Hutson and practice specialist Deb Reynolds in attendance with Gregory Einhorn (telephonically), and in person, Carolyn Erickson and Jay Short of Diversa Corporation. However, after the Examiner has reviewed the instant response and amendment, if the Examiner believes a telephonic interview would help expedite prosecution, please call Applicants' representative at (858) 720-5133.

a. Status of the Claims

Pending claims

Claims 1 to 17 and 28 to 44 are pending.

B. Claims canceled and added in the instant amendment

Claim 45 is added and claims 13 to 15 are canceled, without prejudice or disclaimer. Thus, after entry of the instant amendment, claims 1-12, 16-17 and 28 to 45 will be pending.

Claims 34 to 35 and 38 have been withdrawn. In the instant office action claim 44 is withdrawn, the Patent Office alleging that newly added claim 44 is drawn to an invention that is independent or distinct from the elected invention. Thus, claims 1-12, 16-17, 28-33, 36-37 and 39-43 will be pending and under consideration.

Outstanding Rejections

Claims 16 and 17 stand rejected under 35 U.S.C. §112, second paragraph. Claims 4-17 and 39-43, are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification. Claims 1-17, 28-33 and 36-37 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Claims 4-15, 17 and 39-43 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086.

Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

The Restriction Requirement

In the instant office action, the Patent Office alleges that claim 44 (added in Applicants' last response, dated January 20, 2004, is drawn to an invention that is independent or distinct from the elected invention. Applicants respectfully traverse.

Reasons to reconsider and withdraw restriction requirement

Applicants respectfully request the Patent Office to reconsider and to withdraw the instant restriction requirement for the following reasons.

Applicants respectfully aver that after a search directed to isolated or recombinant nucleic acids comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, it would not be an undue burden for the Patent Office to also complete a search for methods for producing a biologically active polypeptide and screening the polypeptide for enhanced activity comprising use of a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity. Accordingly, Applicants respectfully request rejoining of claim 44 to the elected Group I.

Applicants respectfully request that, after the elected product claims have been found to be allowable, all withdrawn process (methods) claims which depend from or otherwise include all of the limitations of the allowed product claims be rejoined. MPEP §821.04; pg 800-63, 8th Edition, Aug. 2001/ revision Feb. 2003; In re Ochiai, 37 USPQ2d 1127 (Fed. Cir. 1995); In re Brouwer, 37 USPQ2d 1663 (Fed. Cir. 1995); 1184 OG 86, 3/26/96.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the amended claims. Support for claims directed to nucleic acids having a sequence with at least about 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, or at least 50% sequence identity (homology) to an exemplary nucleic acid of the invention and fragments comprising at least about 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto, can be found,

inter alia, in the paragraph spanning pages 42 and 43, and lines 9 to 15 of page 43. Support for claims directed to methods for producing a biologically active polypeptide and screening the polypeptide for enhanced activity can be found, inter alia, on line 30, page 26 to line 9, page 31.

Issues under 35 U.S.C. §112, second paragraph

Claims 16 and 17 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The instant amendment addresses the objections to claims 16 and 17.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 4 to 6, 7 to 17 and 39 to 43, are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

With regard to claims 4 to 6 and 7 to 17, the Patent Office alleged, inter alia, that the Applicants' previous arguments are not commensurate in scope with the claims as these claims purportedly do not incorporate functional limitations. The instant amendment addresses this issue. For example, amended claims 4 and 5 are directed to, inter alia, nucleic acids comprising a sequence encoding a polymerase, where the nucleic acid hybridizes to a sequence as set forth in SEQ ID NO:1 under specific hybridization and wash conditions. Amended claims 8 to 10 are directed to, inter alia, nucleic acids that encode a polymerase, where the nucleic acids have a specific sequence identity to SEQ ID NO:1. Amended claim 12 is directed to, inter alia, nucleic acids that encode a polymerase and comprise at least 100 consecutive bases of a sequence as set forth in SEQ ID NO:1, or at least 200 consecutive bases of a sequence having at least 70% identity to SEQ ID NO:1 and encoding a polymerase. Amended claim 16 is directed to nucleic acids encoding a polymerase having a sequence as set forth in SEQ ID NO: 2, or enzymatically active fragments having polymerase activity. Amended claim 17 is directed to nucleic acids encoding a polymerase and

comprising at least 30 consecutive amino acids of a polypeptide having a sequence as set forth in SEQ ID NO: 2, or enzymatically active fragments having polymerase activity.

Support for hybridization and wash conditions

Claims 4 to 6 stand further rejected under 35 U.S.C. §112, first paragraph, as allegedly not supported by the specifically recited hybridization or wash conditions. In response, Applicants respectfully direct the Office's attention to the specification, for example, at page 16, lines 8 to 14; page 40, lines 10 to 19; the paragraph from page 41, line 25 to page 42, lines 4; and, in general the description on pages 41 to 43. Applicants respectfully aver that the specification (for example, in the referenced sections) provides the requisite descriptive support for claims (including claims 4, 5, and 6) directed to nucleic acids defined by their ability to hybridize to exemplary nucleic acids under defined hybridization and wash conditions.

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

Claims 1 to 17, 28 to 33, 36 and 37 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification such that one skilled in the art to which it pertains could make and/or use the invention commensurate in scope with these claims.

The Patent Office states that the specification is enabling for the polynucleotide of SEQ ID NO:1, which encodes a polypeptide having polymerase activity.

As discussed above, the instant amendment addresses the Office's concern regarding functional limitations. The amended claims are directed to nucleic acids encoding polypeptides having polymerase activity.

However, it is alleged, inter alia, that the specification does not provide reasonable enablement for the large number of claimed polymerase-encoding polynucleotides. The Patent Office alleged that it is not routine experimentation to screen for multiple substitutions or multiple modifications as encompassed by the claims. It is alleged that it would have required some knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues,

that correlate with polymerase activity to create variants of an exemplary nucleic acid and test them for the expression of polypeptides having polymerase activity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of polymerases to practice the claimed invention. Applicants respectfully maintain that whether large numbers of compositions (e.g., variants of nucleic acids or proteins) must be screened to determine if one is within the scope of the claims is irrelevant to an enablement inquiry; please see Applicants response of January 20, 2004, e.g., page 18. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). "Time and difficulty" are not determinative of undue experimentation if the experimentation is routine. See PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996). In Hybritech, Inc., the court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners in the art at the time of this invention were prepared to make and screen large numbers of negatives in order to find a sample with the desired properties, e.g., a polymerase-encoding nucleic acid. Those skilled in the relevant art at the time of the instant claimed invention could, using the state of the art and Applicants' written disclosure, produce and screen a genus of nucleic acids of the invention (e.g., nucleic acids having at least , 70%, 80%, 90%, 95% or more sequence identity to SEQ ID NO:1, and having polymerase activity) without undue experimentation. Thus, the making and screening that would be necessary to generate polymerase-encoding nucleic acids, as set forth in the claimed methods, was not "undue experimentation."

"The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The adequacy of a disclosure for meeting the enabling requirement of 35 USC § 112 varies with a number of factors including the predictability

of the art and the breadth of the claims. In re Wands, 858 F.2d 731, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In general, the stringency of the enablement requirement increases with the unpredictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ (BNA) 18, 24 (CCPA 1970). However, even in an unpredictable art, "applicants are not required to disclose every species encompassed by their claims," In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d (BNA) 1438, 1445 (Fed. Cir. 1991) (citing In re Angstadt, 537 F.2d 498, 502-03, 190 USPQ (BNA) 214, 218 (CCPA 1976)), but the disclosure must be sufficient to teach one skilled in the art "how to make and . . . use the invention as broadly as it is claimed." Id. And, the scope of enablement need only present a reasonable correlation to the scope of the claims. *See* e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Nevertheless, not everything necessary to practice the invention need be disclosed, what is well-known may be omitted. *See* In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

Regarding making the claimed genus of nucleic acids, Applicants respectfully aver that the specification did provide the skilled artisan a reasonable amount of guidance. For example, on page 16, lines 19 to 26, the specification provides guidance on alternative methods for generating the claimed genus of nucleic acids.

As noted above, the Patent Office also remains concerned that because there may be insufficient guidance as to which changes in sequence would be acceptable to retain the desired activity or function, it would be undue experimentation to test (screen for) a large number of variants to determine if a nucleic acid encoded a polymerase and was within the scope of the claimed invention.

Applicants respectfully maintain that the specification did provide the skilled artisan a reasonable amount of guidance with respect to screening for polymerases, i.e., screening variant nucleic acids to identify the claimed genus of polymerase-encoding nucleic acids. For example, Example 1, page 69, line 31, to page 70, describes a protocol to identify and characterize polymerases; including protocols to determine the most favorable conditions for utilizing DNA polymerases of the invention. See also page 11, line 6 to page 12, line 19, where the specification give further guidance regarding determining polymerase activity. Page 15, lines 6 to 12, of the specification notes that polymerase polypeptide sequences of the invention can be assayed for

polymerase biological activity by any number of methods, including polymerizing DNA (e.g., the speed and proofreading accuracy of polymerization). For example an assay for the proofreading accuracy of the invention polymerase can include a comparison of the sequence of a DNA polymerized by the invention polymerase with a known sequence for accuracy, and the like. Accordingly, the specification provides guidance on alternative, routine protocols for determining polymerase activity that can be practiced without undue experimentation.

Furthermore, as declared by Dr. Short in the declaration submitted in Applicants' previous response, the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for polymerase activity was very high. Dr. Short declared that using the teaching of the specification (see discussion, above), one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary polymerases of the invention and screen them for expression of polypeptides having polymerase activities. Dr. Short declared that while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results predictable (i.e., it was predictable to find nucleic acids encoding polymerases having various activities). Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including screening for and identifying the claimed genus of polymerase-encoding nucleic acids.

The Patent Office remains concerned that, inter alia, the specification does not have sufficient guidance to make the claimed genus of polymerase-encoding nucleic acids, e.g., does not establish regions of protein structure which may be modified while producing variants having polymerase activity.

However, Applicants respectfully note that the specification does provide guidance as to what amino acid substitutions can be made to make the genus of polymerases of the invention. For example, the paragraph on page 14, line 26 to page 15, line 5, of the specification, teaches

> ... a "substantially identical" amino acid sequence is a sequence that differs from a reference sequence by one or more conservative or non-conservative amino acid substitutions, deletions, or insertions, particularly when such a substitution occurs at a site that is not the active site of the molecule, and provided that the polypeptide essentially retains its functional properties. A conservative amino acid substitution, for example, substitutes one amino acid for another of the same class (e.g., substitution of one

hydrophobic amino acid, such as isoleucine, valine, leucine, or methionine, for another, or substitution of one polar amino acid for another, such as substitution of arginine for lysine, glutamic acid for aspartic acid or glutamine for asparagine). One or more amino acids can be deleted, for example, from a polymerase polypeptide, resulting in modification of the structure of the polypeptide, without significantly altering its biological activity. For example, amino- or carboxyl-terminal amino acids that are not required for polymerase biological activity can be removed.

According, the specification did provide guidance as to what amino acid changes could be made to make the genus of claimed polymerases. Furthermore, Applicants respectfully aver that direction to the skilled artisan as to which amino acid residues can be substituted, deleted or inserted into a nucleic acid to obtain structural, and functional, homologues of an enzyme could also be found in the art at the time of the invention. For example, the three dimension structure of polymerases had been described, see, e.g., Wang (1997) Cell 89(7):1087-1099; Eom (1995) Acta Crystallogr. D. Biol. Crystallogr. 51(Pt 6):1086-1088, thus providing direction as to which amino acid residues can be modified and how structure correlates with function. Furthermore, at the time of the invention one of skill in the art would have been aware of the many studies of polymerase activity and active sites, see, e.g., Blasco (1993) J. Biol. Chem. 268(22):16763-16770, "Phi 29 DNA polymerase active site"; Blasco (1995) J. Biol. Chem. 270(6):2735-2740, "Primer terminus stabilization at the phi 29 DNA polymerase active site. Mutational analysis of conserved motif KXY"; de Vega (1997) J. Mol. Biol. 270(1):65-78, "An invariant lysine residue is involved in catalysis at the 3'-5' exonuclease active site of eukaryotic-type DNA polymerases."

Accordingly, one skilled in the art at the time of the invention, using the teaching of the specification (and including the teaching of the specification), had many sources of direction to determine which amino acid residues could be substituted, deleted or inserted into a nucleic acid to obtain structural, and functional, homologues of a polymerase enzyme.

However, Applicants respectfully aver that it would not have been necessary for one skilled in the art to understand which specific regions of polymerase structure could be modified to generate the genus of nucleic acids or polypeptides of the invention. As noted by Dr. Short in his previously submitted Rule 132 declaration, it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with

polymerase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides or peptides having polymerase activity.

The Patent Office has cited art that allegedly shows the "unpredictability of assigning function based on structural homology and how small changes can lead to major changes in function." Please see the Office action mailed August 20, 2003, page 12, lines 1 to 3, citing Ngo, et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al. (Ed.) ("Ngo"); and, (reference AU, IDS submitted July 18, 2003) Colman, Res. In Immunology, vol. 145, no. 1, pp. 33 to 36, "Effects of amino acid sequence changes on antibody antigen interactions" ("Coleman").

In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). See also MPEP §2164.04, rev. 2, May 2004, pg 2100-189.

The examiner must weigh all the evidence before him or her, including the specification and any new evidence supplied by applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled. The examiner should never make the determination based on personal opinion. The determination

should always be based on the weight of all the evidence. MPEP §2164.05, 8th edition, rev. 2, May 2004, pg 2100-190 to -191.

Applicants respectfully aver that the examiner has not met his or her initial burden to establish a reasonable basis to question the enablement provided for the claimed invention, and specifically address, below, how the art used to support the Office's enablement rejection is not sufficient to rebut the presumptively enabled specification.

Additionally, because the examiner must weigh all the evidence before him or her, the Office did not sufficiently consider and specifically address Dr. Short's previously submitted Rule 132 expert declaration regarding enablement, in which Dr. Short declared, inter alia, that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with polymerase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides or peptide having polymerase activity, with reasons to doubt the objective truth of the statements contained therein. Applicants respectfully aver that their arguments, and Dr. Short's expert declaration, are sufficient to rebut any possible *prima facie* case of lack of enablement, i.e., Applicants have presented persuasive arguments that one skilled in the art would be able to make and use the claimed invention using the application as a guide. The evidence provided by applicant need not be conclusive but merely convincing to one skilled in the art. MPEP 2164.05, 8th edition, rev. 2, May 2004, pg 2100-190 to -191.

As noted above, the Patent Office cited Ngo and Coleman to allegedly support that "the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity or function and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e., its activity) are not well understood and are not predictable." However, none of these references, individually or in their totality, are sufficient to rebut the presumption of enablement. None of these references are directed to whether, or not, screening a large number of nucleic acid variants (of an exemplary nucleic acid of the invention) would have constituted undue experimentation to one skilled in the art at the time of the invention.

Coleman appears to be cited to support the statement that "the relationship between the sequence of a peptide and its tertiary structure (i.e., its activity) are not well understood and are not predictable." Coleman does opine on the effects of amino acid sequence changes on antibody-

antigen binding, noting that conservative or non-conservative amino acid substitutions can effect the ability of an antibody to bind to antigen. However, in Coleman, there is no discussion regarding the merits or difficulties of protocols that screen for enzyme activity, e.g., screen for enzyme activity in a library of polypeptides expressed by a plurality of nucleic acid variants. In fact, it appears that Coleman considered screening for antibody-antigen binding a routine process. Coleman emphasized that binding interactions in the "active site", or antigen binding site, of an antibody are less tolerant to change, noting that for protein antigens the surface size of the antibody's antigen binding site is about 15 amino acid residues. Thus, Coleman suggests that most changes in an antibody's amino acid sequence (e.g., non-antigen binding site residues) are not important in determining, or changing, its binding activity.

Ngo is a review chapter from a 1994 publication that opines that, at least as of 1994, there was no efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. However, the polymerase activity of the exemplary SEQ ID NO:1 of the invention is not based on sequence identity homology to known proteins, but rather are based on empirical, experimental data demonstrating that it has activity (see, e.g., Example 1, pages 69 to 70, of the specification). Additionally, as discussed above, by the time of the instant invention one of skill in the art would have been aware of many publications directed to polymerase active sites and polymerase three-dimensional structures.

Applicants respectfully aver that none of these references, individually or in their totality, are sufficient to rebut the instant application's presumption of enablement. None of these references are directed to whether, or not, screening a large number of nucleic acid variants would have constituted undue experimentation to one skilled in the art at the time of the invention. In fact, because Colman and Ngo's data suggest that most changes in a polypeptide's amino acid sequence (e.g., non-binding or non-catalytic site amino acid residues) are not important in determining, or changing, binding or catalytic specificity, these references support the idea that most changes in a polypeptide's amino acid sequence will result in little or no effect on its specificity or activity, and that one of skill in the art could easily target a minimum number of residues to generate a limited number of enzyme variants to generate desired active (enzyme) variants.

In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Gelfand, et al., U.S. Patent No. 5,491,086

Claims 4 to 15, 17 and 39 to 43 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086 (*Gelfand*). It is alleged that *Gelfand*, et al., teaches a nucleic acid 66.5% identical to the exemplary SEQ ID NO:1 of the invention, and, the DNA taught by *Gelfand* comprises many regions of at least 10 consecutive bases of a sequence as set forth in SEQ ID NO:1 and encodes a polypeptide comprising at least 10 consecutive amino acids of SEQ ID NO:2.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131.

The Office alleges that claims 4 to 17 are not limited to a genus of nucleic acids which encode a polymerase and that they "are merely drawn to nucleic acids which are described structurally, but lack any functional limitations." As discussed above, the instant amendment addresses this issue. The amended claims are directed to nucleic acids encoding polypeptides having polymerase activity.

The Patent Office specifically alleges that *Gelfand* anticipates claims 4 to 6 drawn to a recombinant nucleic acid comprising a sequence that hybridizes to a nucleic acid having a sequence as set forth in SEQ ID NO:1 under specified conditions. The Patent Office is concerned that because claims 4 to 6 are not limited to nucleic acids of any particular length, they may be anticipated by *Gelfand*. The present amendments to claims 4 and 5 address this issue by addition of the stringent hybridization wash conditions limitation. The claimed nucleic acids will not hybridize to the nucleic acid taught by *Gelfand*, which is 66.5% identical to the instantly disclosed SEQ ID NO:1. New claim 45 also addresses this issue; it is directed a polymerase-encoding nucleic acid that hybridizes across the entire length of SEQ ID NO:1.

The Patent Office also alleges that *Gelfand* anticipates claims 7 to 11, or claims drawn to a recombinant nucleic acid having at least 70% to 95% sequence identity to a nucleic acid having at least 70% sequence identity to SEQ ID NO:1 and encoding a polymerase. The instant amendments to claims 7 to 10 address this concern. Amended claims 1, 8, 9 and 10 are directed to polymerase-encoding nucleic acids having at least 70%, 80%, 90% or 95%, respectively, sequence identity to the exemplary SEQ ID NO:1 (not to a nucleic acid having at least 70% sequence identity to SEQ ID NO:1). As confirmed by Applicants, and noted by the Office, *Gelfand* teaches a nucleic acid having only 66.5% sequence identity to SEQ ID NO:1.

The Patent Office also alleges that *Gelfand* anticipates claim 12, drawn to a nucleic acid comprising at least 20 consecutive bases of SEQ ID NO:1, and claims 13 to 15, drawn to nucleic acids at least 70, 80%, or 90% identical to at least 20 consecutive bases of SEQ ID NO:1. The instant amendment addresses this issue. Claim 12 is directed to nucleic acids encoding polypeptides having polymerase activity comprising at least 100 consecutive bases of a sequence as set forth in SEQ ID NO:1, or, at least 200 consecutive bases of a sequence having at least 70% identity to SEQ ID NO:1 (claims 13 to 15 are canceled, without prejudice or disclaimer). *Gelfand* does not teach a polypeptide having polymerase activity comprising at least 100 consecutive bases of SEQ ID NO:1 or at least 200 consecutive bases of a sequence having at least 70% identity to SEQ ID NO:1.

The Patent Office alleges that *Gelfand* anticipates claim 17, drawn to a nucleic acid encoding a polymerase comprising at least 20 consecutive amino acids of SEQ ID NO:2. The present amendment to claim 12 overcomes this rejection. Amended claim 12 is directed to nucleic acids encoding a polypeptide having polymerase activity and comprising at least 30 consecutive amino acids of a polypeptide having a sequence as set forth in SEQ ID NO:2. *Gelfand* does not teach a polypeptide comprising at least 30 consecutive amino acids of SEQ ID NO:2, as confirmed by the alignment provided by the Office.

The Patent Office alleges that claims 39 to 43 are anticipated by *Gelfand* because this reference purportedly teaches methods for making a polypeptide comprising expressing the taught nucleic acids in an expression vector, and prokaryotic and/or yeast host cells. Claim 39 is directed to a method for making a polypeptide comprising: (a) providing a nucleic acid having a sequence

set forth in claim 1 or claim 12; and (b) expressing the sequence, thereby expressing the polypeptide. As discussed above, the instant amendment addresses the Patent Office's concerns regarding claim 12 (and it is not alleged that claim 1 is anticipated by *Gelfand*). Accordingly, because *Gelfand* does not teach the limitations of claims 1 or 12, it cannot then anticipate the methods of claims 39-43.

Applicants respectfully submit that the instant amendment addresses all of the Patent Office's concerns regarding *Gelfand* and claimed invention. Thus, the rejection under section 102(b) can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs and 35 U.S.C. §102(b). Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952 referencing docket no. 564462001613. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference and interview with the Examiner, and, after the Examiner has reviewed the instant response and amendment, to expedite prosecution of this application have invited the Examiner to call the undersigned representative at (858) 720-5133.

Dated: August 25, 2004

Respectfully submitted,

By _____

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